

<sup>2</sup>  
58. (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

*Sub H2*  
59. (Amended) A method according to claim 57, wherein the hedgehog compound is an Indian hedgehog protein or fragment thereof which binds to *patched*.

60. (Amended) A method according to claim 80, wherein the TGF- $\beta$  compound is a bone morphogenic protein.

<sup>17</sup>  
~~61.~~ (Amended) A method according to claim <sup>16</sup>~~60~~, wherein the bone morphogenic protein is BMP-2, BMP-4, BMP-6, or BMP-7.

<sup>4</sup>  
~~62.~~ (Amended) A method according to claim <sup>1</sup>~~57~~, further comprising maintaining the cell population in vitro in a culture medium, and wherein contacting the cells with a hedgehog compound includes contacting the cells with a culture medium comprising the hedgehog compound.

<sup>5</sup>  
~~63.~~ (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the undifferentiated mesodermally derived cells are hematopoietic stem cells.

<sup>6</sup>  
~~64.~~ (Amended) A method according to claim <sup>5</sup>~~63~~, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.

<sup>7</sup>  
~~65.~~ (Amended) A method according to claim <sup>5</sup>~~63~~, wherein the hematopoietic stem cells are obtained from adult bone marrow cells.

<sup>8</sup>  
~~66.~~ (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the cells are progenitor cells obtained from an adult human.

<sup>9</sup>  
~~67.~~ (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the cells comprise embryonic tissue.

<sup>10</sup>  
68. (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the cells comprise an embryonic explant culture.

E4  
cont <sup>11</sup>  
69. (Amended) A method according to claim <sup>10</sup>~~68~~, wherein the embryonic explant culture is a blastocyst.

<sup>12</sup>  
70. A method according to claim <sup>1</sup>~~57~~, wherein the cells are hematopoietic stem cells within the bone marrow of an animal.

<sup>14</sup> ~~71~~. (Amended) A method according to claim <sup>1</sup>~~57~~, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.

E5  
E <sup>13</sup>  
72. (Amended) A method according to claim <sup>12</sup>~~70~~, wherein contacting the stem cells with the hedgehog compound includes administering an effective dose of the compound to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.

sub 72  
73. (Amended) A method according to claim 80, wherein the TGF- $\beta$  compound enhances the stimulation of hematopoiesis of the cells by more than the amount of stimulation of hematopoiesis resulting from administration of an identical amount of the TGF- $\beta$  compound in the absence of the hedgehog compound.

Please add the following new claims:

R.1.126  
15 <sup>80</sup>  
80. (New) A method according to claim <sup>1</sup>~~57~~, further comprising contacting the cells with a TGF- $\beta$  compound.

E6  
sub 73  
81. (New) A method of stimulating hematopoiesis in an animal, comprising administering to the animal a hedgehog compound comprising a polypeptide sequence at least 80% identical to a sequence selected from SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37,

SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

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82. (New) A method according to claim 81, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

But 74 83  
83. (New) A method according to claim 81, further comprising contacting the cells with a TGF- $\beta$  compound.

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84. (New) A method according to claim 83, wherein the TGF- $\beta$  compound is a bone morphogenic protein.

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85. (New) A method according to claim 84, wherein the bone morphogenic protein is selected from BMP-2, BMP-4, BMP-6, and BMP-7.

But 75 86  
86. (New) A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo hematopoiesis, comprising contacting the cells with a hedgehog compound comprising a polypeptide sequence of SEQ ID NO: 41, SEQ ID NO: 42, or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

Sub H 87  
87. (New) A method according to claim 86, wherein the undifferentiated mesodermal-derived cells are a population of hematopoietic stem cells.

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88. (New) A method according to claim 87, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.

Es 28  
89. (New) A method according to claim 87, wherein the cells are human progenitor cells.

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90. (New) A method according to claim 87, wherein the cells are hematopoietic stem cells within the bone marrow of the animal.

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(New) A method according to claim 87, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.

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(New) A method according to claim 81, wherein an effective dose of the hedgehog compound is administered to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.

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93.

(New) A method of stimulating hematopoiesis in an animal, comprising administering to the animal a hedgehog compound comprising a polypeptide sequence of SEQ ID NO: 41, SEQ ID NO: 42, or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

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94.

(New) A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo hematopoiesis, comprising contacting the cells with a hedgehog compound so as to stimulate the cells to undergo hematopoiesis, wherein the hedgehog compound comprises a polypeptide sequence encoded by a nucleic acid which hybridizes under stringent conditions, including a wash step of 0.2 x SSC at 65 °C, to a nucleic acid sequence designated in one of SEQ ID Nos. 27-33, which polypeptide sequence binds to *patched* and induces cells to undergo hematopoiesis.

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95.

(New) A method according to claim 94, wherein the hedgehog compound is an Indian hedgehog, Desert hedgehog, or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis.

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96.

(New) A method according to claim 94, wherein the hedgehog compound is an Indian hedgehog protein or fragment thereof which binds to *patched*.

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97.

(New) A method according to claim 94, further comprising contacting the cells with a TGF- $\beta$  compound.

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108. (New) A method according to claim 97, wherein the TGF- $\beta$  compound is a bone morphogenic protein.

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109. (New) A method according to claim 98, wherein the bone morphogenic protein is BMP-2, BMP-4, BMP-6, or BMP-7.

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110. (New) A method according to claim 94, further comprising maintaining the cell population in vitro in a culture medium, and wherein contacting the cells with a hedgehog compound includes contacting the cells with a culture medium comprising the hedgehog compound.

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111. (New) A method according to claim 94, wherein the undifferentiated mesodermally derived cells are hematopoietic stem cells.

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112. (New) A method according to claim 101, wherein the hematopoietic stem cells are selected from cord blood cells, fetal liver cells, and peripheral blood cells.

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113. (New) A method according to claim 101, wherein the hematopoietic stem cells are obtained from adult bone marrow cells.

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114. (New) A method according to claim 94, wherein the cells are progenitor cells obtained from an adult human.

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115. (New) A method according to claim 94, wherein the cells comprise embryonic tissue.

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116. (New) A method according to claim 94, wherein the cells comprise an embryonic explant culture.

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117. (New) A method according to claim 106, wherein the embryonic explant culture is a blastocyst.

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(New) A method according to claim 94, wherein the cells are hematopoietic stem cells within the bone marrow of an animal.

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(New) A method according to claim 94, wherein the cells are hematopoietic stem cells present in the animal in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.

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(New) A method according to claim 109, wherein contacting the stem cells with the hedgehog compound includes administering an effective dose of the compound to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.

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(New) A method according to claim 97, wherein the TGF- $\beta$  compound enhances the stimulation of hematopoiesis of the cells by more than the amount of stimulation of hematopoiesis resulting from administration of an identical amount of the TGF- $\beta$  compound in the absence of the hedgehog compound.

*The claims presented above incorporate changes as indicated by the marked-up versions below.*

57. (Amended) A method of stimulating a population of undifferentiated mammalian mesodermally derived cells to undergo [at least one of] hematopoiesis[, endothelial cell differentiation and proliferation], comprising[:]

[(a) providing a first compound selected from the group consisting of hedgehog and WNT and optionally a second compound comprising a TGF- $\beta$ ; and

(b)] contacting the cells with [the one or more compounds] a hedgehog compound so as to stimulate the cells to undergo [at least one of] hematopoiesis, [endothelial differentiation and endothelial proliferation] wherein the hedgehog compound comprises a polypeptide sequence at least 80% identical to a sequence selected from SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, or a fragment thereof which binds to patched and induces cells to undergo hematopoiesis.

58. (Amended) A method according to claim 57, wherein the hedgehog compound is [selected from the group consisting of] an Indian hedgehog, Desert hedgehog, [and] or Sonic hedgehog protein or a fragment thereof which binds to *patched* and induces cells to undergo hematopoiesis [compound].

59. (Amended) A method according to claim 57, wherein the hedgehog compound is an Indian hedgehog protein or fragment thereof which binds to *patched* [compound].

60. (Amended) A method according to claim [57] 80, wherein the TGF- $\beta$  compound is a bone morphogen[et]ic protein[s].

61. (Amended) A method according to claim [57] 60, wherein the bone morphogen[et]ic protein is [selected from the group consisting of] BMP-2, BMP-4, BMP-6, or [and] BMP-7.

62. (Amended) A method according to claim 57, further comprising [the step of] maintaining the cell population in vitro in a culture medium, and wherein [such that step (b) includes] contacting the cells with a hedgehog compound includes contacting the cells with a culture medium comprising the hedgehog compound [in the culture medium].

63. (Amended) A method according to claim 57, wherein the undifferentiated mesodermally [-] derived cells are [a population of] hematopoietic stem cells.

64. (Amended) A method according to claim [57] 63, wherein the hematopoietic stem cells are selected from [the group consisting of] cord blood cells, fetal liver cells, and peripheral blood cells.

[67] 65. (Amended) A method according to claim [65] 63, wherein the hematopoietic stem cells are obtained from adult bone marrow cells.

[68] 66. (Amended) A method according to claim 57, wherein the cells are progenitor cells obtained from an adult human.

[69] 67. (Amended) A method according to claim 57, wherein the cells [constitute] comprise embryonic tissue.

[70] 68. (Amended) A method according to claim 57, wherein the cells [constitute] comprise an embryonic explant culture.

[71] 69. (Amended) A method according to claim [70] 68, wherein the embryonic explant culture is a blastocyst.

[72] 70. A method according to claim 57, wherein the cells are hematopoietic stem cells within the bone marrow of an animal.

[73] 71. (Amended) A method according to claim 57, wherein the cells are hematopoietic stem cells present in the animal [and are selected from the group of hematopoietic cells found] in at least one of bone marrow, cord blood cells, fetal liver cells and peripheral blood cells.

[74] 72. (Amended) A method according to claim [72] 70, [further comprising; causing the compound to] wherein contacting the stem cells with the hedgehog compound includes [by] administering an effective dose of the compound to the animal by any of oral, intradermal, subcutaneous, transmucosal, intramuscular, or intravenous routes.

[75] 73. (Amended) A method according to claim [57] 80, wherein [the first compound is capable of acting synergistically with] the [second] TGF- $\beta$  compound [so as to] enhances the stimulation of [at least one of] hematopoiesis of the cells by more than the amount of stimulation of hematopoiesis resulting from administration of an identical amount of the TGF- $\beta$  compound in the absence of the hedgehog compound [, endothelial cell proliferation and endothelial cell differentiation].

#### **REMARKS**

Claims 57-73 and 80-111 constitute the pending claims in the present application. Misnumbered claims 67-81 are hereby renumbered as claims 65-79, and accordingly the first new claim added herein is presented as claim 80. Applicants respectfully request reconsideration